Claims

1. A method for generating SH3 domains with tailored binding properties, comprising

a) producing a collection of SH3 domains containing a randomized RT-loop (RRT-SH3 domains),

b) generating recombinant libraries expressing said RRT-SH3 domains,

c) subjecting such libraries to affinity or functional selection steps to identify novel SH3 domains.

2. The method according to claim 1, wherein step a) is effected by replacing amino acid residues in the variable region of the RT-loop by any other amino acid residues.

3. The method according to claim 2, wherein said amino acid residues in the variable region of the RT-loop are the six amino acid residues corresponding to the residues 69 to 74 (EAIHHE) in the human Hck protein sequence.

4. The method according to claim 1, wherein the recombinant libraries are selected from plasmid, phagemid and viral libraries.

5. An artificial SH3 domain, wherein amino acid residues in the variable region of its RT-loop have been replaced with any other amino acid residues.

6. The artificial SH3 domain according to claim 5, wherein said amino acid residues in the variable region of its RT-loop are the six amino acid residues corresponding to the residues 69 to 74 (EAIHHE) in the human Hck protein sequence.

7. An artificial SH3 domain derived from Hck-SH3 and targeted to the HIV-1 Nef protein, wherein the peptide motif EAIHHE in the variable region of its RT-loop has been replaced with a peptide motif selected from XSWSXX, XSPFXX and XSXFPW, wherein X is any amino acid.

8. The artificial SH3 domain according to claim 7, wherein X is selected from V, F, D, M, P, S, T, W and Y.

9. The artificial SH3 domain according to claim 8, wherein the peptide motif is selected from VSWSPD, FSWSDT, DSWSTS, YSWSDM, WSPFPS, DSPFSF, FSPFSF, FSPFDW, SSPFDW, YSPFSW, TSPFPW, YSPFPW, YSDFPW and DSWFPW.

10. An artificial SH3 domain derived from Hck-SH3 and targeted to the HIV-1 Nef protein, wherein the peptide motif EAIHHE in the variable region of its RT-loop has been replaced with a peptide motif selected from SSFYSS, QGFLDQ, NAFLPS, EAWSPL, and ESYSEW.

11. A method for inhibiting, activating, or otherwise modifying the functions of cellular or pathogen-encoded proteins for research or therapeutic purposes, comprising expressing RRT-SH3 domains or derivatives thereof in cells comprising such proteins.

12. A diagnostic method for detecting an infectious organism, comprising detecting the binding of an RRT-SH3 domain or a derivative thereof to proteins of such an infectious organism.

13. A method for identifying novel protein targets for drug development, comprising expressing an RRT-SH3 domain or a derivative thereof in a cell to alter the behaviour of said cell, and identifying an SH3-target protein involved in the altered function of said cell.

14. A method for identifying suitable molecular surfaces in known SH3 ligand proteins for guiding drug development, comprising using a RRT-SH3 domain or a derivative thereof to recognize the molecular region in its target protein that should be targeted by a drug in order to prevent similar interactions of this protein with naturally occurring SH3 domains.

15. A method for rational designing of drugs, comprising providing structural data of an RRT-SH3 domain or a derivative thereof, and designing drug candidates structurally mimicking said RRT-SH3 domain and sharing similar binding properties with said RRT-SH3 domain.

16. Method for identifying novel SH3 target proteins, comprising detecting the ability of proteins of interest to bind to an RRT-SH3 domain functionally selected as described in claim 1, or to a derivative thereof.